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Editorial

Free triiodothyronine, not thyroid stimulating hormone, should be focused on for risk stratification in acute decompensated heart failure

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Cardiologists will think it just that thyroid dysfunction would be associated with many cardiovascular diseases [1–3]. In particular, adverse effects of low free triiodothyronine (fT3) level in cardiovascular diseases have already been reported [3–5]. However, among the cardiovascular diseases, previous reports have demonstrated that chronic heart failure and thyroid function are not consistently associated [4–9]. Thyroid stimulating hormone (TSH) did not show consistent prognostic value in chronic heart failure [7,8]. Moreover, there is no previous report clearly indicating the significant importance of thyroid function in the treatment of acute decompensated heart failure (ADHF). Considering such an insufficient state, at first, it is necessary to assess whether we could separate the adverse outcome of ADHF patients by thyroid function on admission or not.

In this issue of the *Journal of Cardiology* [10], Okayama et al. investigated the association between thyroid hormone levels [TSH, fT3, and free thyroxine (fT4)] and outcome in 270 patients hospitalized for ADHF. Receiver operating characteristics (ROC) curve analysis revealed the most favorable performance of fT3 (area under the ROC curve: 0.791, sensitivity 85.0%, specificity 72.0%). Interestingly, multivariate analysis indicated that low fT3 level was independently associated with higher in-hospital mortality (odds ratio 14.4). The probability of 1-year total death among patients with low fT3 was significantly higher than that among patients with normal fT3. These results are suggestive and provide meaningful clinical implications. The authors have special knowledge in clinical studies and the treatment for heart failure in a major Japanese cardiovascular center, and the present study design, aim, and statistic analysis are reasonable and organized. Considering the present results, as concluded by the authors, we also say with conviction that low fT3 level was associated with adverse outcomes in patients hospitalized for ADHF, and that fT3 measurements should be done for the risk stratification of ADHF patients. Furthermore, it is suggestive that the prognostic value in ADHF patients is superior in fT3 than in TSH, because thyroid hormone action in the myocardium is via specific T3 receptors, and low fT3 levels may worsen contractility, increase susceptibility to arrhythmias, and contribute to mortality in patients with heart failure despite normal T4 and TSH levels [14].

We should discuss whether low fT3 level is a target or severity marker of ADHF. Low fT3 levels must induce heart failure, because thyroid hormones affect various organs and cells and are associated with maintenance of normal cardiac function [1–9,11,12]. Actually, low fT3 was associated with pulmonary capillary wedge pressures, and lower ejection fraction [2]. Previous studies have demonstrated that fT3 increases tissue thermogenesis, cardiac contractility, heart rate, and cardiac output, and decreases systemic vascular resistance including that of the coronary artery [1,12,13]. Considering these results, low fT3 would be a therapeutic target of ADHF, and a previous clinical study has demonstrated the benefits of short-term T3 replacement on advanced heart failure [15]. However, we are afraid that long-term T3 replacement could cause unexpected inotropic effects, and we should determine the causal importance of hypothyroidism in ADHF patients, because the proportion of hypothyroidism in pathophysiology is not uniform and has dynamic features. In addition, hypothyroidism is also induced by various systemic organ damages in heart failure. As discussed by the authors, cachexia and/or poor nutritional status have recently been focused on as topics in heart failure, and these topics are strongly mediated by hypothyroidism, especially low fT3 levels. Although the present paper could not conclude whether thyroid function is the target or a severity marker of ADHF, cardiologists had better consider low fT3 levels, at least, as a useful clinical marker of severity and risk stratification in ADHF patients.

As the authors already acknowledge, the present paper is a single-center observational study with a limited number of study patients, and the measurement of thyroid hormone was not performed in all ADHF patients. Considering these study limitations, the present paper could not provide data on the prevalence and prognostic impact of persisting thyroid function abnormality on ADHF patients. To strengthen the authors' concept, time course of low fT3 levels in ADHF patients and more detailed assessment of ADHF (echocardiographic, hemodynamic, and exercise tolerance test) are expected in the future following studies. However, the present authors' clinical message is suggestive, and we should focus on low fT3, not TSH, in ADHF patients more and more.

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